

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Catherine Dulac and Richard Axel
Serial No. : Not Yet Known
Filed : Herewith
For : CLONING OF VERTEBRATE PHEROMONE RECEPTORS
AND USES THEREOF

1185 Avenue of the Americas
New York, New York 10036
July 3, 2001

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

PRELIMINARY AMENDMENT AND INFORMATION DISCLOSURE STATEMENT

Please amend the subject application as follows:

In the specification:

On page 1, please delete the paragraph on lines 6-9 and replace it with the following new paragraph:

--This application claims the benefit of U.S. Serial No. 08/731,745, filed October 18, 1996, which claims the benefit of U.S. Provisional Application No. 60/005,698, filed October 19, 1995, the contents of both of which are incorporated by reference into the subject application.--

On page 19, line 15, please add the following three paragraphs:

--This invention provides an isolated nucleic acid comprising consecutive nucleotides encoding a vertebrate pheromone receptor protein, wherein the receptor protein comprises seven transmembrane domains and is further characterized by at least one of the following characteristics:

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- (a) the loop between the second and third transmembrane domains of the protein, the third transmembrane domain, and the loop between the third and fourth transmembrane domains together comprise consecutive amino acids having the following sequence: -R, G, L or F, S or T or N, L, C or S, A or T, T or A or S, C, L or M, L, S or N or H, V or I, L or F, Q or W, A or T or M, I or F, I or T, L, S, P or S, R or K, S or K, S, C, L, A or T, K or T, F or Y, K, H or Y, K or N- (SEQ ID NO: 19);
 - (b) the loop between the fifth and sixth transmembrane domains of the protein, and the sixth transmembrane domain together comprise consecutive amino acids having the following sequence: -K, A or S or V, S, P, E or Q, Q, R, A, T, R or Q or E, T or S, I, L or M, M or L or I, L, M or R, S or T, F or L, F, V or G, V or L- (SEQ ID NO: 20); and
 - (c) the seventh transmembrane domain of the protein comprises consecutive amino acids having the following sequence: -Y, A, T, V or I or L, S, P or S, F or L, V or L, F or L- (SEQ ID NO: 21).--

--In one embodiment, the receptor protein is characterized by at least two of the characteristics of (a) through (c). In one embodiment, the receptor protein is characterized by all of the characteristics of (a) through (c).--

--This invention provides an isolated nucleic acid comprising consecutive nucleotides encoding a vertebrate pheromone receptor protein, wherein the nucleic acid encodes a protein selected from the group consisting of:

- i) VN1 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 8,

- ii) VN2 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 9,
- iii) VN3 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 10,
- iv) VN4 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 11,
- v) VN5 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 12,
- vi) VN6 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 13,
- vii) VN7 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 14, and
- viii) a protein that shares between 47% and 87% amino acid sequence identity with any one of the proteins of i) - vii).--

On page 29, line 28, please add the following the following paragraph:

--A method of preparing a composition which comprises identifying a compound using any of the methods described herein, recovering the compound free of any pheromone receptor, and admixing the compound with a pharmaceutically acceptable carrier.--

On pages 63-89, please delete the SEQUENCE LISTING and replace it with the SEQUENCE LISTING attached hereto as **EXHIBIT 1**.

In the claims:

Please cancel claims 1-28 and 33-93 without prejudice to applicants' right to pursue the subject matter of these claims in a future continuation or divisional application.

Please add new claims 96-99 as follows:

--96. (New) An isolated nucleic acid comprising consecutive nucleotides encoding a vertebrate pheromone receptor protein, wherein the receptor protein comprises seven transmembrane domains and is further characterized by at least one of the following characteristics:

(a) the loop between the second and third transmembrane domains of the protein, the third transmembrane domain, and the loop between the third and fourth transmembrane domains together comprise consecutive amino acids having the following sequence: -R, G, L or F, S or T or N, L, C or S, A or T, T or A or S, C, L or M, L, S or N or H, V or I, L or F, Q or W, A or T or M, I or F, I or T, L, S, P or S, R or K, S or K, S, C, L, A or T, K or T, F or Y, K, H or Y, K or N- (SEQ ID NO: 19);

(b) the loop between the fifth and sixth transmembrane domains of the protein, and the sixth transmembrane domain together comprise consecutive amino acids having the following sequence: -K, A or S or V, S, P, E or Q, Q, R, A, T, R or Q or E, T or S, I, L or M, M or L or I, L, M or R, S or T, F or L, F, V or G, V or L- (SEQ ID NO: 20); and

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--97. (New) The isolated nucleic acid of claim 96, wherein the receptor protein is characterized by at least two of the characteristics of (a) through (c).--

--98. (New) The isolated nucleic acid of claim 97, wherein the receptor protein is characterized by all of the characteristics of (a) through (c).--

--99. (New) The isolated nucleic acid of claim 96, wherein the nucleic acid encodes a protein selected from the group consisting of:

- i) VN1 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 8,
- ii) VN2 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 9,
- iii) VN3 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 10,
- iv) VN4 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 11,

- v) VN5 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 12,
- vi) VN6 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 13,
- vii) VN7 protein comprising consecutive amino acids having a sequence identical to the sequence set forth in SEQ ID NO: 14, and
- viii) a protein that shares between 47% and 87% amino acid sequence identity with any one of the proteins of i) -vii).--

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REMARKS

Claims 1-95 were pending in the subject application. By this Amendment applicants have canceled claims 1-28 and 33-93 without prejudice or disclaimer, and added new claims 96-99. Accordingly, upon entry of this Amendment, claims 29-32 and 94-99 will be pending and under examination.

Applicants maintain that the amendments to the application do not raise any issue of new matter. Applicants have amended page 1 of the specification to update the continuing data for the subject application. Support for the additions to page 19 of the specification and for new claims 96-99 may be found inter alia in the specification, as originally-filed, on page 15, lines 20-28; page 19, lines 2-3; page 37, lines 30-31; and in Figure 4A. Support for the addition to page 29 may be found inter alia in the specification, as originally-filed, on page 22, lines 17-22, and page 29, lines 24-27. Applicants have replaced the original Sequence Listing with a new Sequence Listing which includes the sequences recited in new claim 96. Accordingly, applicants respectfully request that this Amendment be entered.

Applicants submit herewith as **Exhibit 3** a Sequence Listing in a computer readable form which complies with the requirement of 37 C.F.R. §1.824. In addition, applicants submit a Statement in Accordance with 37 C.F.R. §1.821(f), attached hereto as **Exhibit 2**, certifying that the computer readable form containing the nucleic acid and/or amino acid sequences as required by 37 C.F.R. §1.821(e) contains the same information as the paper copy of the Sequence Listing attached hereto as **Exhibit 1**.

Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (**Exhibit A**) and which were previously cited in connection with the prosecution of U.S. Serial Number 08/731,745 from which the subject application claims priority under 35 U.S.C. §120. According to 37 C.F.R. §1.98(d), copies of patents or publications that were previously cited by, or submitted to, the Office in connection with such prior applications need not accompany the Information Disclosure Statement. Accordingly, copies of the following references are not attached to this Information Disclosure Statement:

1. U.S. Patent No. 5,278,141, issued January 11, 1994, Berliner;
2. U.S. Patent No. 5,508,164, issued April 16, 1996, Kausch et al;
3. U.S. Patent No. 5,576,210, issued November 19, 1996, Sledziewski et al.;
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If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

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Applicants are submitting this Information Disclosure Statement under 37 C.F.R. §1.97(b)(1) with the filing of a national application. Accordingly, no fee other than the enclosed \$355.00 fee for filing the subject application is deemed necessary in connection with the filing of this Preliminary Amendment and Information Disclosure Statement. However, if an additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully Submitted,



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